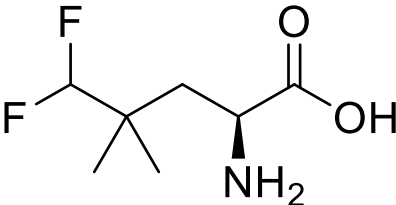


Product data sheet



MedKoo Cat#: 555979 Name: NV-5138 CAS: 2095886-80-7 Chemical Formula: C ₇ H ₁₃ F ₂ NO ₂ Exact Mass: 181.0914 Molecular Weight: 181.1828	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years. In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

NV-5138 is an orally and centrally active small-molecule drug for the treatment of major depressive disorder (MDD). It directly and selectively activates the mammalian target of rapamycin complex 1 (mTORC1) signaling pathway by binding to and modulating sestrin2, a leucine amino acid sensor and upstream regulatory pathway. The mTORC1 pathway is the same signaling pathway that the NMDA receptor antagonist ketamine activates in the medial prefrontal cortex (mPFC) to mediate its rapid-acting antidepressant effects. A single oral dose of NV-5138 has been found to increase mTORC1 signaling and produce synaptogenesis in the mPFC and to induce rapid antidepressant effects in multiple animal models of depression.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under “QC And Documents” section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	25.0	137.98

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	5.52 mL	27.60 mL	55.19 mL
5 mM	1.10 mL	5.52 mL	11.04 mL
10 mM	0.55 mL	2.76 mL	5.52 mL
50 mM	0.11 mL	0.55 mL	1.10 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of “Calculator”

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Sengupta S, Giaime E, Narayan S, Hahm S, Howell J, O'Neill D, Vlasuk GP, Saiah E. Discovery of NV-5138, the first selective Brain mTORC1 activator. *Sci Rep.* 2019 Mar 11;9(1):4107. doi: 10.1038/s41598-019-40693-5. PMID: 30858438; PMCID: PMC6412019.

In vivo study

1. Kato T, Pothula S, Liu RJ, Duman CH, Terwilliger R, Vlasuk GP, Saiah E, Hahm S, Duman RS. Sestrin modulator NV-5138 produces rapid antidepressant effects via direct mTORC1 activation. *J Clin Invest.* 2019 Apr 16;129(6):2542-2554. doi: 10.1172/JCI126859. PMID: 30990795; PMCID: PMC6546461.

2. Sengupta S, Giaime E, Narayan S, Hahm S, Howell J, O'Neill D, Vlasuk GP, Saiah E. Discovery of NV-5138, the first selective Brain mTORC1 activator. *Sci Rep.* 2019 Mar 11;9(1):4107. doi: 10.1038/s41598-019-40693-5. PMID: 30858438; PMCID: PMC6412019.

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7. Bioactivity

Biological target:

NV-5138, a leucine analog, is the first selective and orally active brain mTORC1 activator, binding to Sestrin2.

In vitro activity

This study reports NV-5138, a novel orally bioavailable compound that binds to Sestrin2 and activates mTORC1 both in vitro and in vivo. Treatment with NV-5138 activates mTORC1 in leucine-starved unedited HEK-293T cells, but not in cells lacking all three Sestrins or the GATOR1 component Npr13 indicating that compound activity requires an intact Sestrins/GATOR pathway (Fig. 2f,g).

Reference: Sci Rep. 2019 Mar 11;9(1):4107. <https://pubmed.ncbi.nlm.nih.gov/30858438/>

In vivo activity

The results demonstrate that a single dose of NV-5138 produced rapid and long-lasting antidepressant effects, and rapidly reversed anhedonia caused by chronic stress exposure. The antidepressant actions of NV-5138 required BDNF release as the behavioral responses are blocked by infusion of a BDNF neutralizing antibody into the medial prefrontal cortex (mPFC) or in mice with a knock-in of a BDNF polymorphism that blocks activity dependent BDNF release. NV-5138 administration also rapidly increased synapse number and function in the mPFC, and reversed the synaptic deficits caused by chronic stress.

Reference: J Clin Invest. 2019 Apr 16;129(6):2542-2554. <https://pubmed.ncbi.nlm.nih.gov/30990795/>

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.